

PATENT COOPERATION TREATY
PCT

INTERNATIONAL SEARCH REPORT
(PCT Article 18 and Rules 43 and 44)



Applicant's or agent's file reference 12424680/TDO/FT	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/AU2004/000336	International filing date (<i>day/month/year</i>) 18 March 2004	(Earliest) Priority Date (<i>day/month/year</i>) 18 March 2003
Applicant MEDVET SCIENCE PTY. LTD. et al		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☒ Certain claims were found unsearchable (See Box No. II).

3. ☐ Unity of invention is lacking (See Box No. III).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

A method of modulating smooth muscle cell functioning by modulating sphingosine kinase mediated signalling

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☒ none of the figures is to be published with the abstract.

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A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. ⁷: C12Q 1/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

SEE ELECTRONIC DATABASE BOX BELOW

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SEE ELECTRONIC DATABASE BOX BELOW

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CA, MEDLINE, WPIDS: Keywords: smooth muscle, sphingosine, RhoA, Rho kinase, signal transduction, regulate, modulate, inhibit, express.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	Bolz S-S <i>et al.</i> (2003) Circulation 108: 342-347. "Sphingosine kinase modulates microvascular tone and myogenic responses through activation of RhoA/Rho kinase" See whole document.	1-52
P, X	Dantas A P V <i>et al.</i> (2003) Am J Physiol Heart Circ Physiol 284: H2045-H2052. "Sphingosine 1-phosphate and control of vascular tone". See whole document.	1-27 and 45-49
P, X	Rosenfeldt H M <i>et al.</i> (2003) FASEB J 17: 1789-1799. "Sphingosine-1-phosphate stimulates contraction of human airway smooth muscle cells" See whole document.	1-27 and 45-49

☒ Further documents are listed in the continuation of Box C ☐ See patent family annex

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search
28 April 2004

Date of mailing of the international search report
4 MAY 2004

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages (Remove spaces when completed if the page is too long)	Relevant to claim No.
X	Jolly P S <i>et al.</i> (2001) Mol Immunol 38: 1239-1245. "The roles of sphingosine-1-phosphate in asthma" See whole document, especially figures 1 and 4	1-27 and 45-49
X	Ammit A J <i>et al.</i> (2001) FASEB J 15: 1212-1214. "Sphingosine 1-phosphate modulates human airway smooth muscle cell functions that promote inflammation and airway remodeling in asthma" See whole document.	1-27 and 45-49
X	Wettschureck N & Offermanns S (2002) J Mol Med 80: 629-638. "Rho/Rho-kinase mediated signalling in physiology and pathophysiology" See whole document.	1-19, 25 and 26
X	Bitar K N & Yamada H. (1995) Am J Physiol 269: G370-G377. "Modulation of smooth muscle contraction by sphingosylphosphorylcholine" See whole document.	1-27 and 45-49
A	Waters C <i>et al.</i> (2003) J Biol Chem 278(8): 6282-6290. "Sphingosine 1-phosphate and platelet-derived growth factor (PDGF) act via PDGF β receptor-sphingosine 1-phosphate receptor complexes in airway smooth muscle cells" See whole document.	

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 27-44 and 50-52
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
See supplementary box below.
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

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Supplemental Box

(To be used when the space in any of Boxes I to VIII is not sufficient)

Continuation of Box No: II

Claims 27-44 and 50-52 are unduly broad and speculative. These claims refer to the use of agents that modulate the functional effective level of sphingosine kinase. There is no support for what is encompassed within the scope of the term "agent". Therefore it is not feasible to perform a meaningful and economical search on these claims.

Furthermore, these claims do not comply with rule 6.3 of the PCT. This rule refers to the claims defining the technical features of the invention. The invention lies in the determination that sphingosine kinase mediates the signalling pathway that regulates smooth muscle cell tone. Claims 27-44 and 50-52 are not limited to the agents when used to act directly on sphingosine kinase. The agents only have to be capable of modulating sphingosine kinase mediated signalling and then used to prepare a medicament. The medicament may then be used for any purpose. Thus the claims are not limited to the technical features of the invention and therefore the claims were not searched.